IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Muhammad Anzar et al. Art Unit 1651
Serial No. 10/811,593
Filed March 29, 2004
Confirmation No. 2857
For PROCESS FOR THE STAINING OF SPERM
Examiner Tiffany M. Gough

July 6, 2007

COMMISSIONER FOR PATENTS
P.O. BOX 1450
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SIR:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants hereby request review of the Office's rejection of claims 1-38 as set forth in the final Office action dated February 8, 2007. A Notice of Appeal is being filed concurrently herewith.

While no fees are believed due with respect to this Request, the Commissioner is authorized to charge any fees due to Deposit Account No. 19-1345.

ARGUMENTS

For each of the claims discussed below, the Office's rejection fails to establish that the claimed invention is obvious. Specifically, Applicants' discovery that sperm cells can be stained with a dye for use in flow cytometry processes at temperatures ***in excess of 40°C*** in less time than required to stain the cells at lesser temperatures ***without significant negative impact on sperm viability*** facilitated Applicants claimed method of staining viable sperm cells in less time than is required to stain cells at lower temperatures. Before this discovery, as particularly demonstrated by the prosecution history of Johnson, one of the primary 103(a) references cited by the Office, staining at temperatures in excess of 39°C was believed to negatively impact sperm cell viability. Because the knowledge of one of ordinary skill in the art prior to this application was that cells could not be stained at temperatures in excess of 40°C without significantly affecting cell viability, a claimed process of staining viable cells at a temperature in excess of 40°C while maintaining cell viability cannot be demonstrated to be obvious.

A. Claims 1-23 and 29-38 over Seidel et al. or Johnson in view of D'Occhio, Guthrie et al., Garner et al., Sabeur et al., De Pauw et al., Bruemmer et al., or Remington

Claim 1 is directed to a process for staining sperm cells. The process comprises forming a staining mixture containing intact viable sperm cells and a DNA selective fluorescent dye and subjecting the staining mixture to a temperature in excess of 40°C.

Johnson discloses the separation of intact X- and Y-chromosome bearing sperm populations into X- and Y-chromosome bearing sperm enriched populations based on DNA content using flow cytometry. The sperm cells are combined with a DNA selective dye at a temperature of 30°C to 39°C.[1] Johnson discloses incubation for a period of 1 hour at 35°C,[2] 1 hour at 39°C,[3] and 1.5 hours at 30°C.[4] Johnson also discloses a staining and sorting procedure where sperm cells were incubated in 5μM Hoechst 33342 at 35°C for 1 hour.[5]

Particularly telling is the prosecution history of Johnson. In response to a 103(a) rejection, Johnson added the requirement that the sperm cells be incubated at a temperature of about 30°C to 39°C and thereafter ***consistently argued the criticality of the temperature range*** for the purpose of staining the cells sufficiently to discriminate between X- and Y-chromosome bearing cells ***while preserving sperm viability***.[6] Moreover, in response to a 103(a) rejection based in part on the *Handbook of Histopathological and Histochemical Techniques*,[7] disclosing histological mounting and staining techniques, Johnson noted that there were ***no attempts therein to preserve the viability of the stained cells***, stating that "[e]xcept at the ***very low end*** of the 37-57°C range indicated in the reference, sperm cells would immediately be killed."[8]

Almost ***eleven and one-half years after the filing of Johnson***, Seidel et al.[9] filed an application disclosing methods of staining sperm cells to increase the resolution of stained X- and Y-chromosome bearing cells, with ***the focus of achieving this goal on adjustments to the dye concentration and the staining duration***. Notably, however, with respect to staining

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[1] Johnson, U.S. Patent No. 5,135,759, column 4, line 41, and claims 1, 19, and 20.
[2] Johnson, U.S. Patent No. 5,135,759, column 4, line 40, and claims 7 and 25.
[3] Johnson, U.S. Patent No. 5,135,759, column 4, line 43, and claims 6 and 24.
[4] Johnson, U.S. Patent No. 5,135,759, column 4, line 43, and claims 8 and 26.
[5] Johnson, U.S. Patent No. 5,135,759, Example 1, column 6, lines 32-33.
[6] Johnson, U.S. Patent 5,135,759, file history, Amendment of July 26, 1990, at pages 4-5; Amendment of April 26, 1991, at page 7; and Preliminary Response of May 30, 1991, at page 1.
[7] Cullling, Handbook of Histopathological and Histochemical Techniques, 3rd Ed., Butterworths & Co. (1974), page 192.
[8] Amendment of January 16, 1992, at page 10 (emphasis added).
[9] Seidel et al., U.S. Patent Application No. 2004/0049801, filed November 29, 2001. Seidel et al. claim priority to two provisional applications, each of which is stated to have a filing date of November 29, 2000.

temperatures Seidel et al. ***parroted the disclosure of Johnson***, reciting the staining of sperm cells with Hoechst 33342 dye at temperatures between about 30°C and about 40°C. Particular embodiments recite the staining of sperm cells at about 37°C and at about 39°C.[10] While Seidel et al. disclose the effects of ***dye concentration*** and ***staining duration*** on the number of oocytes, the percent cleavage, and the percent blastocysts/oocyte ***in their single working example, there is no disclosure of the temperature at which any of the cell samples were stained.***[11]

Thus, Johnson disclosed that cells may be stained at temperatures from about 30°C to about 39°C, and ***that this temperature range is critical to sperm cell viability***. Seidel et al., reciting essentially the same temperature range as Johnson, effectively reaffirmed the criticality of this range eleven plus years later. Therefore, while one skilled in the art might reasonably conclude that sperm cells may be subjected to staining temperatures in the range of 30°C to 39°C without significant impact on cell viability, the very same skilled individual would have ***no reason*** to conclude that sperm cells could withstand staining temperatures in excess of 40°C without a significantly negative impact on cell viability. Indicative of this is the fact that ***none of the references of record*** discloses staining sperm cells at a temperature in excess of 40°C, even though approximately 70% of the art of record, including Seidel et al., was published ***after*** the publication of Johnson. Simply stated: there is ***no data or evidence of record*** that contradicts Johnson.

Accordingly, staining sperm cells at temperatures in excess of 40°C as presently claimed cannot be said to be obvious in light of the disclosure of Johnson or Seidel et al., as these references would indicate to one skilled in the art that (1) the temperature range at which the claimed process is performed is ***in excess of the then known range*** of temperatures for staining sperm cells and (2) the staining of sperm cells at temperatures in excess of the then known range of temperatures would be ***detrimental to sperm cell viability***.

Against this backdrop, it cannot be maintained that the claimed processes are obvious in light of the secondary references the Office combined therewith. While each of D'Occhio,[12] Guthrie et al.,[13] Garner et al.,[14] Sabeur et al.,[15] and DePauw et al.,[16] disclose the staining of

[10] Seidel et al., U.S. Patent Application Publication No. 2004/0049801, paragraph [0037].
[11] Seidel et al., U.S. Patent Application Publication No. 2004/0049801, paragraphs [0049] and [0050] and Table 1.
[12] D'Occhio, Animal Breeding: Use of New Technologies, Chapter 19: 247-264 (1999).
[13] Guthrie et al., Molecular Reproduction and Development, 61(1): 87-92 (2002).
[14] Garner et al., Biology of Reproduction, 53: 276-284 (1995).
[15] Sabeur et al., Journal of Reproduction and Fertility, 120: 135-142 (2000).

sperm cells, Bruemmer et al.[17] disclose the use of pyruvate in a sperm diluent, and Remington et al.[18] disclose the use of vitamin K_3 and the lipoamide-lipoamide dehydrogenase couple as redox agents in a sperm buffer, ***none of these secondary references discloses the staining of viable sperm cells at a temperature in excess of 40°C***. Accordingly, the failure of Johnson and Seidel et al. to render the claimed processes obvious for the reasons stated above is not remedied by the disclosure of any of these secondary references, either alone or in combination, as each and every element of the claimed invention is not present in the cited art when combined. As such, a *prima facie* case of obviousness has not been established.

B. Claims 1-15, and 24-28 over Seidel et al. or Johnson in view of Van Demark et al. or Salisbury et al.

Van Demark et al.[19] discloses a storage diluent containing sodium citrate dihydrate, sodium bicarbonate, potassium chloride, glucose, sulfanilamide, penicillin dihydrostreptomycin sulfate, and sufficient egg yolk to make a final diluent consisting of 10% to 15% egg yolk and saturated with CO_2 (termed "IVT diluter") that maintains the motility of sperm stored in it.

Salisbury et al.[20] disclose the collection of bull ejaculates into collection diluent A consisting of 1.4926g $NaHCO_3$, 0.9231g $KHCO_3$, and 1.890g $C_6H_8O_7 \cdot H_2O$ in water (100ml), collection diluent B consisting of 0.8146g $NaHCO_3$, 1.7301g $KHCO_3$, and 1.890g $C_6H_8O_7 \cdot H_2O$ in water (100ml), and control diluent C consisting of 0.9% NaCl. The air phase above diluents A and B was replaced by gassing with 100% carbon dioxide, while the phase above diluent C was air. It is disclosed that cells collected in diluent A were immotile within about two hours, while cells collected in diluent B were immotile upon immediate examination after collection, remaining so for several hours at room temperature and for at least eight days at 5°C.

For the reasons stated above, Johnson and Seidel et al. fail to disclose each and every element of the claimed process and fail to demonstrate that Applicants merely optimized a known process. Van Demark et al. or Salisbury et al. do nothing to remedy this deficiency, as Van Demark et al. and Salisbury et al. merely disclose diluents for sperm storage. Neither reference discloses staining viable sperm cells at a temperature in excess of 40°C.

Moreover, Van Demark et al. and Salisbury et al. utilize the disclosed buffers as storage

[16] De Pauw et al., Biology of reproduction, 67: 1073-1079 (2002).
[17] Bruemmer et al., Journal of Animal Science, 80(1): 12-18 (2002).
[18] Remington et al., International Application Publication No. WO 02/077011.
[19] Van Demark et al., U.S. Patent No. 3,005,756.
[20] Salisbury et al., Journal Reproductive Fertility, 6: 351-359 (1963).

buffers, and in particular, for storage periods of ***one or more days***. Applicants' claimed process is for the staining of sperm cells – a process that occurs in a matter of minutes to several hours. Nothing in the cited art would indicate to one skilled in the art the need to use a "storage buffer," and in particular one that is disclosed to be useful for storing sperm cells for multiple days, in a process that takes at most several hours. Indicative of this is the fact that neither Johnson nor Seidel et al., the two primary references used to support the Office's obviousness rejections, suggest such a concept – even in light of the fact that these references were filed or had a priority date that is approximately ***30 years*** (Johnson) and ***40 years*** (Seidel et al) ***after*** the publication of Van Demark et al. and Salisbury et al. In the absence of being able to demonstrate the obviousness of Applicants' claimed invention based on the cited art, the Office has instead utilized Applicants' specification as a template for achieving the claimed invention. This form of "hindsight," however, is neither permissible nor the standard for determining obviousness.[21]

As such, a *prima facie* case of obviousness has not been established.

Claims 2-23 and 29-34, which depend from claim 1, and claims 2-15 and 24-28, which depend from claim 1, are patentable over Seidel et al. or Johnson in view of D'Occhio, Guthrie et al., Garner et al., Sabeur et al., De Pauw et al., Bruemmer et al., or Remington et al. and over Seidel et al. or Johnson in view of Van Demark et al. or Salisbury et al. for the reasons stated with respect to claim 1 and by reason of the additional requirements each claim introduces.

CONCLUSION

For at least these reasons, Applicants respectfully request allowance of all pending claims.

Respectfully submitted,

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[21] *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1532 (Fed. Cir. 1988); *In re Yates*, 663 F.2d 1054, 1057, 211 U.S.P.Q. 1149, 1151 (C.C.P.A. 1981).